Remarks

Interview

Applicant thanks the Examiner for an in-person interview that took place on February 4, 2008, at which the present rejections were discussed. The Examiner indicated that amending the claims to recite particular microparticle components (*e.g.*, using Markush language) and to recite "pharmaceutical" or "diagnostic" agents would be sufficient to overcome the rejection under § 112 for alleged lack of enablement. Furthermore, the Examiner suggested that the new matter rejection under § 112 could be overcome by pointing to the specification for support for exclusion of synthetic polymers from claimed microparticles and/or compositions thereof. The Examiner and the Applicant also discussed the rejections under § 103, and the Examiner agreed that Bernstein does not indicate using a mixture of blend of lipid, protein, and sugar to form a microparticle matrix, as recited by the present claims.

Applicant notes that the Interview Summary, mailed February 8, 2008, indicates that the interview took place on February 5, 2008. Applicant respectfully submits that the interview took place on February 4, 2008, and requests that the record be corrected to reflect this date.

Status of the Claims

Claims 1, 7-47, 58-65, 80, 84-91, and 96-98 are pending in the application. Claims 1, 7-20, 23-25, 27, 28, 30, 37, 46, 47, 58-65, 80, 84-91, and 96-98 stand rejected.

Previously withdrawn claims 21, 22, 26, 29, 31-36, and 38-45 have been canceled by the present Amendment. Claims 28, 46, and 85 are also canceled by the present Amendment.

Claims 1, 7-15, 17, 62-65, 86-89, 90, 91, and 96-98 have been amended. Claims 1, 62, and 86 have been amended to include Markush groups reciting specific lipids, proteins, and sugars and to recite a pharmaceutical agent. Claim 86 has been amended to recite a solid microparticle instead of a pharmaceutical composition and to eliminate repetitive language. Claims 63 and 90 have been amended to depend from claim 1 or 101. Claims 7-15, 17, 63-65, 87-89, and 96-98 have been amended to correct the antecedent bases of these claims. Claims 91 and 96-98 have been amended to correct the dependencies of these claims.

Support for the amendments to claims 1, 62, and 86 can be found in original claims 28 and 46; and in the specification on page 12, lines 4-19; page 16, line 4; page 16, line 22-page 17,

line 1; and page 18, line 21 to page 23, line 9. Support for the amendment to claim 86 can be found in the specification on page 16, line 4; and page 16, line 22 to page 17, line 1.

New claims 99-107 have been added. Support for new claim 99 can be found in the specification on page 12, lines 5-11. Support for new claim 100 can be found in the specification on page 12, lines 1-2. Support for new claims 101 and 103 can be found in original claims 28 and 46; and in the specification on page 16, line 4; page 16, line 22 to page 17, line 1; page 18, line 21 to page 23, line 9; and page 12, line 20 to page 13, line 3. Support for new claim 102 can be found in the specification on page 12, line 20 to page 13, line 3. Support for new claim 104 can be found in original claims 28 and 46; and in the specification on page 12, line 20 to page 13, line 3; page 16, line 4; and page 16, line 22 to page 17, line 1. Support new claim 105 can be found in original claim 25. Support new claim 106 can be found in original claim 30. Support new claim 107 can be found in original claim 37.

No new matter has been added by the present Amendment. Applicant specifically reserves the right to pursue the subject matter of the canceled or amended claims in a related application. The present Amendment is introduced for the sole purpose of furthering prosecution. Applicant respectfully requests reexamination and reconsideration of the case in light of the present Amendments and the following remarks. Each of the rejections levied in the Office Action is addressed individually below.

Rejection under 35 U.S.C. § 112, for lack of enablement

Claims 1, 7, 11-14, 16-18, 23, 62, 63, 86-91, and 96-98 stand rejected under 35 U.S.C. § 112, for lack of enablement. The Examiner states that the specification, while being enabling for PLGA, albumin, muscimol, phospholipids, glucose oxidase, insulin, lactose, cellulose bupivacaine, tetraciane, lidocaine, dibucaine, mepivacaine, emulsifier and surfactant, does not reasonably provide enablement for all agents, lipids, proteins, sugars, vasodilators, anticonvulsants, diagnostic agents, prophylactic agents, and synthetic polymers. Applicant respectfully disagrees.

As discussed during the interview, the Examiner indicated that the present rejection would be overcome by amending the claims to recite specific components of microparticles and/or pharmaceutical compositions thereof (*e.g.*, by using Markush language). Therefore, as suggested by the Examiner, Applicant has amended claims 1, 62, and 86 to include Markush

language reciting specific microparticle components. Also as suggested by the Examiner, Applicant has amended claims 1, 62, and 86 to recite "pharmaceutical agent" instead of "agent." Applicant has added new claim 101 that is identical to presently amended claim 1 except that it recites "diagnostic agent." Applicant has added new claim 103 that is identical to presently amended claim 62 except that it recites "diagnostic agent." Applicant has added new claim 104 that is identical to presently amended claim 86 except that it recites "diagnostic agent." As discussed during the Interview, such amendments should overcome the rejection under § 112 for lack of enablement. Applicant, therefore, respectfully requests that the rejection be removed.

Rejection under 35 U.S.C. § 112, for lack of written description

Claims 1, 7-47, 58-65, 80, 84-91, and 96-98 stand rejected under 35 U.S.C. § 112, for lack of written description. The Examiner states that the original specification does not envision a microparticle composition that is not a liposome or does not comprise a synthetic polymer. Applicant respectfully disagrees. During the Interview, the Examiner indicated that the rejection could be overcome by specifically pointing to the specification for support for exclusion of synthetic polymers and liposomes.

Applicant respectfully submits that the specification *does* describe microparticle compositions that do not comprise synthetic polymers. For example, page 3 of the specification describes "a system for delivering an agent encapsulated in a lipid-protein-sugar matrix to an individual" (lines 8-9). The specification further states, "In *another* particularly preferred embodiment, a synthetic polymer is substituted for at least one of the components of the LPSPs–lipid, protein, and/or sugar" (emphasis added; page 3, lines 16-18). Page 14 of the specification reiterates this point, stating "The agent is preferably encapsulated in a matrix comprising lipid, protein, and sugar to form microparticles…In *other* embodiments, a synthetic polymer…is used as a substitute for at least one of the components of the LPSPs [*i.e.* lipid, protein, sugar]" (emphasis added; lines 7-8 and 12-15). Thus, the specification clearly describes LPSPs that do not comprise synthetic polymers as distinct from particles which do comprise synthetic polymers. Clearly, the inventors at the time of filing envisioned microparticles that do not include synthetic polymers.

Furthermore, the specification exemplifies both LPSPs and particles comprising synthetic polymers and shows that LPSPs which do not comprise synthetic polymers are superior to

particles comprising synthetic particles. Specifically, particles containing PLGA were shown to elicit a statistically significant increased inflammatory response at the site of injection compared to lipid-protein-sugar particles (page 52, sections entitled "Tissue reaction two weeks after injection" and "Tissue reaction eight weeks after injection"). There were no similar adverse findings in rats injected with LPSPs. Given the negative consequences of administering a drug via microparticles comprising a synthetic polymer, the present specification not only *describes* particles that do not include a synthetic polymer, as discussed above, but also *teaches away* from particles that contain synthetic polymers.

Applicant respectfully submits that the specification *does* describe microparticles that are not liposomes. As discussed with the Examiner during the interview, the methods described in the specification for making microparticles are not methods that can be used to produce liposomes. For example, "spray drying, single and double emulsion solvent evaporation, solvent extraction, phase separation, [and] simple and complex coacervation" (page 23, lines 13-14) are methods that produce solid microparticles, as recited by the present claims. Such methods does not produce liposomes. Therefore, the specification does describe solid microparticles which are not liposomes, as recited in the claims.

For all of the reasons outlined above, recitation of LPSPs which do not comprise synthetic polymers and are not liposomes is fully supported by the specification and does not constitute new matter. Applicant, therefore, respectfully requests that the rejection be removed.

Rejections under 35 U.S.C. § 103(a)

Claims 1, 2, 7, 12-20, 23-25, 27, 28, 30, 37, 46-65, 80, 84-91, and 96-98 stand rejected under 35 U.S.C. § 103(a) on the ground that they are unpatentable over Bernstein *et al.* (U.S. Patent 6,423,345). The Examiner states that the particles of the present invention are obvious in view of Bernstein. Applicant disagrees.

The specification of Bernstein does not teach microparticles comprising lipid, protein, and sugar. As acknowledged by the Examiner in the Interview Summary, "While Bernstein lists a number of materials that can form the matrix, Bernstein does not indicate using mixture or blend (*sic*) of those materials for the matrix." Bernstein does include lipids, proteins, and sugars in a list of many different components that can be used to form a polymeric matrix (column 4, lines 19-22). However, Bernstein does not indicate (or even hint) that the specific combination

of these three particular components (*i.e.*, lipids, proteins, and sugars) should be selected as matrix components. As acknowledged by the Examiner during the interview, there is absolutely no suggestion in Bernstein to pick and choose the combination of lipid, protein, and sugar to prepare microparticles, as recited by the present claims. Given that Bernstein clearly describes copolymers, mixtures, and blends of synthetic polymers (column 4, line 8), biodegradable polymers (column 4, lines 17-18), and non-biodegradable polymers (column 4, line 30), the fact that Bernstein *does not* describe blends or mixtures of lipids, proteins, or sugars is positive proof that Bernstein does not describe and, indeed, does not contemplate, blends or mixtures of lipid, protein, and sugar. Applicant, therefore, submits that the present claims are not rendered obvious by the teachings of Bernstein and respectfully requests that the rejection be removed.

Claims 8-11 stand rejected by the Examiner under 35 U.S.C. § 103(a) on the ground that they are unpatentable over Bernstein *et al.* (U.S. Patent 6,423,345) in view of Goldenheim *et al.* (U.S. Patent 6,534,081).

The Examiner only cites Goldenheim for teaching an anesthetic as the agent in the particles. As discussed above, Bernstein does not render obvious the claimed microparticles of the present application, and the combination of Goldenheim and Bernstein also does not teach the claimed microparticles. The claimed microparticles do not include a synthetic polymer. Therefore, even if there is a teaching or suggestion to combine Goldenheim and Bernstein, the combination would not render the claimed invention of claims 8-11 obvious because the references, even when combined, teach a matrix comprising a synthetic polymer. In fact, the combination of references teaches away from the claimed invention because the claimed microparticles do not include a synthetic polymer. Applicant, therefore, respectfully requests that the rejection be removed.

Conclusion

For all of the reasons set forth above, each of the rejections in this case should be removed and the application should proceed to allowance. A Notice to that effect is respectfully requested.

If, at any time, it appears that a phone discussion would be helpful, the undersigned would greatly appreciate the opportunity to discuss such issues at the Examiner's convenience. The undersigned can be contacted at (617) 248-5215.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,

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